

## REMARKS

Claims 1-22 were presented for examination. Claims 6, 10, 11 and 20-22 were withdrawn from consideration.

Claims 1 and 7 were rejected under §112, first paragraph. Claims 1-5, 7-9, and 12-19 were rejected under §112, second paragraph. Claims 1, 5, 7, 9, 12-19 were rejected under §102(b) as being anticipated by Stamler et al. Claims 1-5, 7-9, 12-19 were rejected under §103(b) as being unpatentable over Stamler et al. in view of Lamont and Katz et al.

a. §112, first paragraph rejections

Independent claims 1 and 7 have been amended to delete the word “prevent” and to insert the words --inhibit the occurrence of--.

Further, applicants assert that enablement is provided by the state of the art and would be understood by one of ordinary skill in the art.

Khachigian et al. and Schmidt et al. teach that antioxidants such as NAC block activation of transcription factor NF kappa beta and cytokines TNF alpha of IL-1. That TNF alpha and IL-1 produce preterm labor is taught by Romero et al. and Silver et al. These teachings provide sufficient enablement to allow for the practice of the present invention. Furthermore, it is known that in humans preterm delivery is associated with increased fetal consumption of plasma endogenous antioxidants (Buhimschi et al., Am. J. Obstet. Gynecol.). This teaching provides sufficient enablement to allow for any agent which induces production of endogenous free radical scavengers. It would not be ingenuity beyond that expected of one of ordinary skill in the art to perform experimentation to administer an agent that induces production of endogenous antioxidants and by this reduce the occurrence of preterm delivery.

b. §112, second paragraph rejections

The claims (1-5, 7-9, and 12-19) have been amended to state --an amount effective to inhibit said occurrence or improve said outcome-- (in claims 1-5) or --an amount effective to inhibit said premature rupture-- (in claims 7-9), or --an amount effective to improve said outcome of preterm deliveries-- (in claims 12-19). One of ordinary skill in the art would know without undue experimentation what amounts of the free radical scavenger, or precursor thereto, would yield these results. The applicants assert that experimentation to administer different doses of free radical scavenger to a pregnant animal and measure endogenous antioxidants in plasma and amniotic fluid using the TRAP (total radical antioxidant potential) is not ingenuity beyond that to be expected of one of ordinary skill in the art.

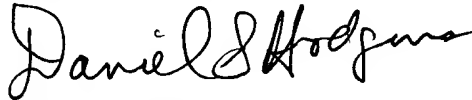
c. §102 and §103 rejections

The Examiner perceives overlap with the teaching of Stamler et al. (U.S. Patent No. 5,648,393) who claims the use of S-nitroso-N-acetylcysteine (a modified N-acetylcysteine) and S-nitroso glutathione to relax smooth muscle. The present claims are distinct of that provided by Stamler et al. who uses the compounds named above as relaxants of uterine muscle and through this halts preterm labor (i.e., a tocolytic agent). The present invention does not require the necessity of a direct relaxant effect on uterine muscle which Stamler suggests to be an effect of the release of nitric oxide. Data presented in the application shows the nitric oxide releasing compounds (S-nitroso penicillamine, SNAP) in point do not prevent the activation of matrix metalloproteases but N-acetyl cysteine does. Stamler uses N-acetylcysteine and glutathione as carrier for nitric oxide as his teaching refers to nitric oxide preventing preterm delivery by reducing the occurrence of uterine contractions (tocolytic). This is fundamentally different from the present invention where the free radical scavenger need not be a tocolytic agent per se.

Further, multiple, more recent studies demonstrate that nitric oxide donors are no better than placebos for the treatment of preterm labor.

The applicant respectfully asks the Examiner to reconsider the amended claims in light of the arguments presented. The applicant asks that the Examiner issue a Notice of Allowance. If the Examiner believes that he needs further explanation, he is invited to contact the undersigned attorney to discuss this Amendment and Response further.

Respectfully submitted,  
JACKSON WALKER L.L.P.

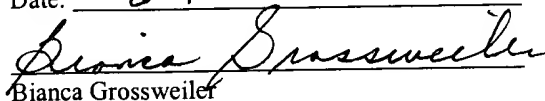


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CERTIFICATE OF MAILING

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited on the date shown below with the United States Postal Service, with sufficient postage as First Class Mail (37 CFR 1.8(a)), in an envelope addressed to Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450.

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